Original Article

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A Study to Know the Effect of Intravenous Methyl Prednisolone Compared to Placebo on Hemodynamics in Patients with Long Bone Fracture of Lower Limb

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Abstract

Background: Fat embolism syndrome (FES) is a potentially lethal condition most commonly seen in polytrauma patients with multiple long-bone fractures. Treatment has centered on supportive care and early fracture fixation. Several small clinical trials have suggested corticosteroids benefit patients with FES, but this treatment remains controversial. Our objective was to determine the effect of corticosteroids on hemodynamic changes with respect to FES in patients with long-bone fractures. *Methods:* Forty four adults, who had sustained a tibia fracture, or a femoral fracture, were subjected to a double-blind randomized study to determine the effect of intra venous methylprednisolone in comparison with placebo on hemodynamic changes with respect to the development of the fat embolism syndrome. A Lindeque2 s criterion for the diagnosis of the fat embolism syndrome was used. *Results:* Post operatively there was significant decrease in the heart rate in methylprednisolone group of patients compared with placebo group. Other parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP) did not show any significant results. *Conclusion:* Prophylactic corticosteroids can be used to prevent changes in vital parameters/ hemodynamic and to manage development of fat embolism syndrome.

Keywords: Fat embolism syndrome; Hemodynamics; Polytrauma .

Introduction

Fat embolism syndrome (FES) is an infrequent clinical consequence, arising from the systemic manifestations of fat emboli within the micro-circulation. Fat embolization is characterized by release of fat droplets into systemic circulation after a traumatic event, which cause direct tis-sue damage as well as induce a systemic inflammatory response resulting in pulmonary, cutaneous, neurological, and retinal symptoms. (1,2)

'Fat embolism syndrome' is a serious manifestation of fat embolism phenomenon characterized clinically by triad of dyspnoea, petechiae and mental confusion. In 1873, Bergmann was first to establish the clinical diagnosis of fat embolism syndrome. (3) Hypoxia is common after long bone fractures and may pass unnoticed.(4) There is no clinical or experimental study until now to demonstrate beneficial effect of any drug on the clinical course of the syndrome,(5) so that prevention, early diagnosis and adequate symptomatic treatment are the mainstays of treatment of this condition. Several pharmacological agents have been used as prophylactic treatment, such as hypertonic glucose,(6) aspirin,(7) dextrans(7) and corticosteroids with variable results.(8,9,10,11) In several clinical trials the use of corticosteroids in various pulmonary disorders and in FE was proven to be beneficial but their use remains controversial. None of the studies focused on the effect of corticosteroids with hemodynamic variables like heart rate and blood pressure in long bone fractures.

This present study was performed to determine the efficacy of methylprednisolone, in improving the hemodynamic parameters with long bone fractures, during development of FES and to improve prognosis.

Methodology

A randomized double blind placebo-controlled trial was

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performed on 44 patients with long bone fractures in a tertiary care hospital. Patients were diagnosed according Lindeque's criteria for fat embolism syndrome, considering inclusion and exclusion criteria and randomized into two groups. Group A as placebo group, receive placebo treatment with normal saline and Group B as study group, and receive methylprednisolone 30mg/kg over one hour.

The authors were blinded to this allocation of groups and drug administration. Institutional ethical clearance was obtained and written informed consent was taken from all the study subjects (No. HOSMAT/ ECM/ 248/ 2008-09).

Lindeques Criteria [8]

- A sustained PaO_2 of less than 8 k.Pa (60mm of Hg) with FiO_2 0.21.
- A sustained $PaCo_2$ of more than 7.3 k.Pa (55mm of Hg) or pH of less than 7.3
- A sustained respiratory rate of greater than 35breath/min. even after adequate sedation.
- Increased work of breathing judged by dyspnoea use of accessory muscles, tachycardia and anxiety.

Any patient with fracture femur and/or tibia showing one or more of these criteria was judged as having Fat Embolism Syndrome

A number of investigations were carried out on admission (baseline values), and again at 2nd, 3rd hour. Post operative temperature, pulse rate, blood pressure and respiratory rate were measured four-hourly for up-to 24 hours. The presence of any petechiae, and their sites was recorded.

Inclusion Criteria

Patients with closed fracture long bone in lower limb, ASA – I, Age- < 45 years.

Exclusion Criteria

Patients with polytrauma, Patients with head injury and sepsis, Patients associated with fracture ribs and lung contusion, Patients with ischemic heart disease, congenital heart disease, hypertension and valvular heart disease, Patients with blunt injury to thorax, abdomen, head and neck, Patients with cervical spine injury and faciomaxillary injuries, Patients with shock– hemorrhagic, septic, cardiogenic and neurogenic, Patients with vascular injuries, Associated with respiratory system and other medical illness like chronic obstructive airway disease, pneumonia (Aspiration) or lower respiratory tract infection.

Results and Discussion

Forty four patients were enrolled and completed the trial (36 men and 8 women). The age range of the patients was from 16 to 46 years (mean age: group A 26.95 ± 7.33 years and group B 28.78 ± 9.16 years). A study by M. K Mobarakeh et al [9] showed the age range of the patients was from 16 to 55 years (mean age: 27.38 ± 11.04 years). At the end of the study period, 23 patients were in the corticosteroid group and 21 patients to the placebo group. There were no statistically significant differences between the two groups regarding age, sex and fracture site. Similar results found in one study [9].

Table 1 shows measurements of hemodynamic parameters in two groups on admission. This shows that two groups received the patients in same condition and there was no disparity between groups about patient's general status.

The heart rate on admission were 92.90±12beats/ min in Group A patients and 90.96±9.23beats/min in Group B. 24 hours after surgery it has increased significantly in Group A patients i.e. 92.43±20.93 beats/min as compared to Group B (80.91±8.93 beats/ min).

Table 3 depicts that the systolic blood pressure was normal before the surgery. There was significant fall in B.P at 3rd hour of operation in Group A, but post operatively both groups maintained normal B.P for 24 hour.

The diastolic blood pressure does not show any variation between two groups in pre operative, intra operative or post operative period (Table 4).

There were no such studies to show the hemodynamic changes in the long bone fracture patients, who were given prophylactic methylprednisolone as preventing tachycardia or hypotension.

The protective effect of corticosteroids against FES and hemodynamic changes suggests that the two are different stages of the same condition [10, 11]. The clinical manifestations of FES frequently appear 24-48 h after the trauma. However, in the studies evalu-ated, prophylaxis with corticosteroids was initiated at hospital admission [10,11,12]. There is no evidence that, after a diagnosis of FES has been established, specific therapy provides any benefit. Therefore, the treatment is based on clinical support.

Administration of 6 mg/kg up to 90 mg/kg methylprednisolone, divided in six doses at 8 h intervals, initiated directly after patient admission, had reduced the incidence of posttraumatic hypoxaemia and has probably also reduced the incidence of FES. Repeated arterial blood gas analysis over the first 48 h in high-risk patients is extremely valuable in detecting and treating those patients with significant hypoxaemia and FES.

The effects of corticosteroids in all the studies have shown about arterial blood gas analysis and FES. None have focused on hemodynamics i.e heart rate, blood pressure.

Future studies are needed to better assess the hemodynamic as well as arterial blood gases for long-term effects of corticosteroid administration in this patient population.

After 3 hours of start of surgery there was fall in the mean systolic BP in Group A (control group) patients as compared to Group B (study group) patients, and it was statistically significant. This fall in systolic BP may be due to release of tourniquet at the end of surgery in some patients. This was not associated with any significant rise in heart rate.

But the reading at 24th hour after surgery showed a statistically significant rise in heart rate in Group A(Control group) patients as compared to that in Group B (Study group) patients. These changes at 24 hours after surgery in vital parameters suggests the development of Fat Embolism Syndrome in these patients due to fat emboli being released into the systemic circulation secondary to fracture manipulation and reaming of marrow cavity during surgery.

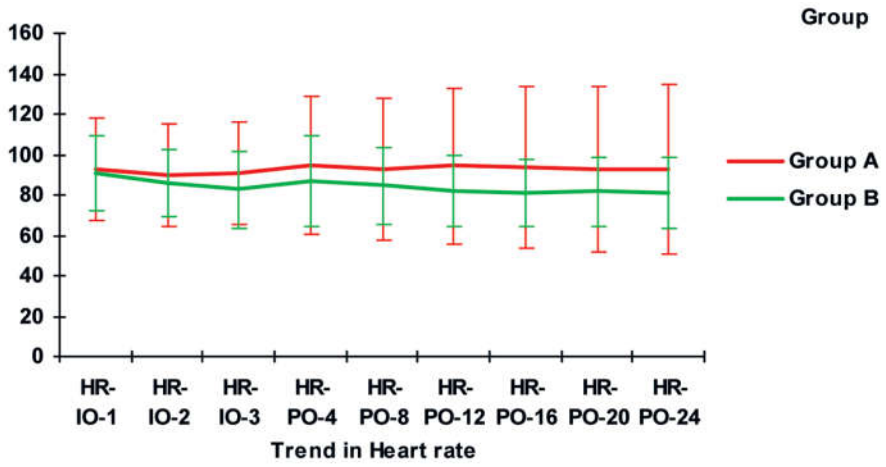
Limitation: The limitation of study is we could not

Table 1: Mean values of hemodynamic parameters on admission in both the groups

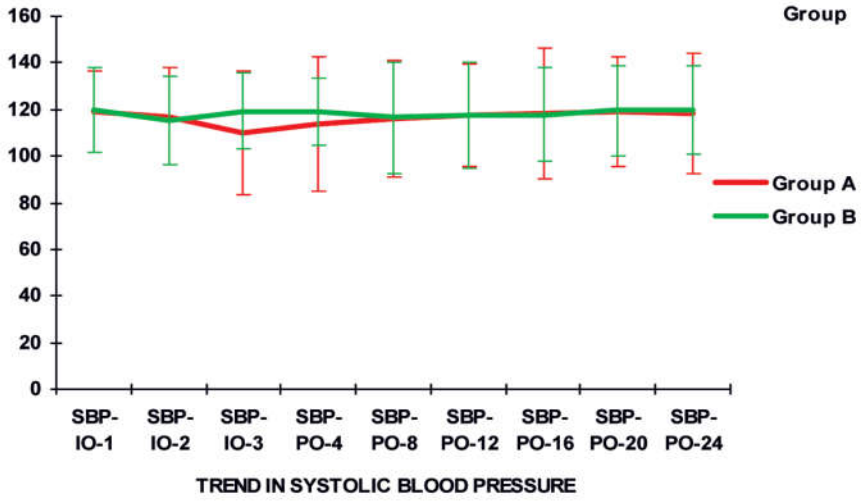
	Heart Rate	Systolic Blood pressure	Diastolic Blood pressure
Group A (n=21)	96.14±16.18	113.81±14.31	76.19±6.69
Group B (n=23)	96.13±13.87	116.96±12.59	76.09±6.56
t	0.002722	0.77143	0.051729
p-value	0.997842	0.444986	0.958995
Statistical significance	N.S.	N.S.	N.S.

Table 2: Mean readings of heart rate in patients at regular intervals

	Intraop 1st Hour	Intraop 2nd hour	Intraop 3rd hour	Postop 4th hour	Postop 8th hour	Postop 12th hour	Postop 16th hour	Postop 20th hour	Postop 24th hour
Group A (n=21)	92.90 ±12.57	89.71 ±12.72	90.71 ±12.80	94.33 ±17.07	92.95 ±17.59	94.19 ±19.10	93.95 ±19.93	92.62 ±20.69	92.43 ±20.93
Group B (n=23)	90.96 ±9.23	85.91 ±8.41	83.78 ±8.33	87.09 ±11.19	84.39 ±9.73	81.96 ±8.69	81.30 ±8.24	81.57 ±8.49	80.91 ±8.93
t	0.58	1.16	2.11	1.65	1.97	2.69	2.70	2.28	2.34
p-value	0.56	0.26	0.04	0.11	0.06	0.01	0.01	0.03	0.03
Statistical significance	N.S.	N.S.	S.	N.S.	N.S.	S.	S.	S.	S.



Graph 1: Trend in heart rate in patients of two groups



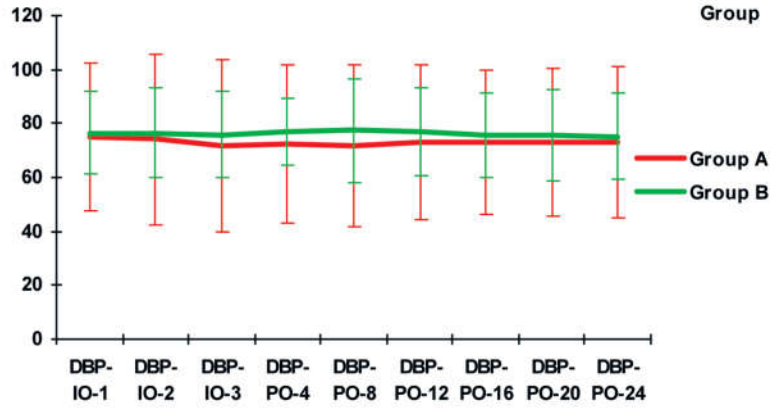
Graph 2: Trend in systolic blood pressure in patients of two groups

Table 3: Readings of systolic blood pressure in patients at regular intervals

	Intraop 1st hour	Intraop 2nd hour	Intraop 3rd hour	Postop 4th hour	Postop 8th hour	Postop 12th hour	Postop 16th hour	Postop 20th hour	Postop 24th hour
Group A (n=21)	119.05 ±8.89	117.14 ±10.56	110.00 ±13.42	115.00 ±13.57	115.71 ±12.48	117.62 ±10.91	118.10 ±14.01	119.05 ±11.79	118.10 ±12.89
Group B (n=23)	120.00 ±9.05	115.22 ±9.47	119.44 ±8.02	119.13 ±7.33	116.52 ±11.91	117.39 ±11.37	117.83 ±9.98	119.57 ±9.76	120.00 ±9.53
t	0.35	0.63	2.71	1.22	0.22	0.07	0.07	0.16	0.55
p-value	0.73	0.53	0.01	0.23	0.83	0.95	0.94	0.88	0.58
Statistical significance	N.S.	N.S.	S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

Table 4: Readings of diastolic blood pressure in patients at regular intervals

	Intraop 1st hour	Intraop 2nd hour	Intraop 3rd hour	Postop 4th hour	Postop 8th hour	Postop 12th hour	Postop 16th hour	Postop 20th hour	Postop 24th hour
Group A (n=21)	77.14 ±7.84	76.67 ±11.11	74.29 ±12.07	74.76 ±9.81	74.48 ±10.52	75.81 ±9.10	75.71 ±7.46	75.71 ±8.11	75.71 ±8.70
Group B (n=23)	76.52 ±7.75	76.52 ±8.32	76.11 ±7.78	76.96 ±6.35	77.39 ±9.64	76.96 ±8.22	75.65 ±7.88	75.65 ±8.43	75.22 ±7.90
t	0.26	0.05	0.57	0.87	0.96	0.44	0.03	0.02	0.20
p-value	0.79	0.96	0.57	0.39	0.35	0.66	0.98	0.98	0.84
Statistical significance	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.



Graph 3: Trend in diastolic blood pressure in patients of two groups

get literatures to cite for the discussion as none of the studies focused on hemodynamics, instead they focused mainly on hypoxemia.

Conclusion

In summary, the current evidence suggests that cortico - steroids may prevent FES in patients with long-bone fractures as well as prevent changes in the hemodynamic parameters. We found no significant differences in the hemodynamic parameters except at the 3rd hour after start of surgery; there was peek fall in systolic pressure.

Based on our findings, which included mostly older and the studies which have not focused on mainly hemodynamic parameters, we would not currently recommend a change in practice. Our findings do, however, provide compelling rationale for the re-evaluation of corticosteroids use in long bone fractures to study effects on hemodynamic parameters. Ultimately, a large confirmatory randomized trial will provide the necessary evidence to guide patient care.

Usefulness

This study can guide us in using prophylactic corticosteroids to prevent changes in vital parameters/ hemodynamic and to manage development of fat embolism syndrome. And also we can find out the dosage of the corticosteroids to administer prophylactically during the long bone fractures patients while admission.

Conflicts of Interest

None

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